
Bilateral Lung Transplantation

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Since its first successful application in 1983, lung transplantation has been employed as a strategy for the treatment of end-stage lung disease. Bilateral-isolated lung transplantation, as opposed to en-bloc heart lung transplantation, was introduced in the late 1980s and the ideal operative approach has evolved continuously.^{1,2} Initially, en-bloc double lung replacement required a median sternotomy, a tracheal anastomosis, and full cardiopulmonary bypass.³ Tracheal anastomotic complications were commonly observed and often fatal. This poor tracheal healing led to the eventual transformation of the operation to include bilateral bronchial anastomoses, performed through a median sternotomy with the anastomoses accomplished in the interaortico-caval space.⁴ The shift of the airway anastomosis from the trachea to the mainstem bronchi improved anastomotic healing, but the anterior mid-line approach hampered access to the posterior mediastinum and made cardiopulmonary bypass necessary for the atrial anastomosis. In 1990, we reported our initial experience with bilateral sequential lung transplantation through bilateral anterior thoracotomies with a joining transverse sternotomy, then referred to as a cross-bow approach.⁵ This approach allowed superior exposure of the pleural space and posterior mediastinum while providing suitable anterolateral exposure for performance of the left atrial anastomosis on both sides. From the start of bilateral sequential lung transplantation at our institution in October 1989 through July 1996, we performed 193 bilateral lung transplants, with the vast majority of these procedures performed as sequential operations through the so-called clamshell or cross-bow thoracosternotomy. The high prevalence of sternal wound complications observed in our patients led us to explore an alternative approach that avoids sternal division. Beginning in July 1996 we began to use bilateral anterolateral thoracotomies without sternal division in selected patients. As our comfort with this exposure increased, we applied this sternal sparing approach to an increasing number of patients and now use this approach routinely. Our results with the sternal sparing incision were recently reported.⁶

The clamshell incision has existed for several decades under various names. Kortz⁷ described it in detail in 1958, stating that, "a bilateral transsternal thoracotomy affords optimal access to the heart and great

vessels, and is of particular value in experimental surgery because it simulates the technical exposure employed in human patients during most intracardiac and pericardiac operations." The authors' use of the clamshell incision for bilateral lung transplantation began in the late 1980s on the advice of Dr Hermes Grillo,⁸ who occasionally employed bilateral anterior thoracotomies with transverse sternal division for resection and reconstruction of the distal trachea and bilateral mainstem bronchi. The superiority of this approach over median sternotomy for lung transplantation was clear, particularly in the improved access it allowed to the posterior mediastinum. The clamshell incision was quickly adopted for bilateral lung replacement and the specific technique was popularized by the Washington University group.⁵

Technical innovation during the first 15 years of successful lung transplantation has resulted in two types of changes: major departures from the original techniques and continuous evolutionary changes that are, in themselves, imperceptible but that cumulatively have shaped modern techniques. If one accepts the single lung transplant (SLT)^{1,9} as the foundation on which innovation is added, major changes have included the arrival and departure of en-bloc double lung transplantation,³ the introduction of the bilateral sequential single lung transplant (BLT),^{4,5} the elimination of the omental pedicle wrap, and the exploration of living related lobar transplantation as a solution to the shortage of cadaveric allograft lungs.^{10,11} Evolutionary changes include the selection of suture material for bronchial and vascular anastomoses, the choice of incisions for single and bilateral lung replacement, and the variety of flush solutions developed for the preservation of graft lungs. This article details the authors' current techniques used in the performance of bilateral lung transplantation.

Selection of Type of Procedure

Once the decision has been made to proceed with lung transplantation, further planning must take place to determine whether a recipient will receive an SLT or a BLT. It is accepted practice that patients with septic lung disease, particularly cystic fibrosis and bronchiectasis, require a BLT to remove the entire focus of sepsis and prevent soiling of the allograft lung with purulence

from the remaining native lung. Lung transplant candidates with obstructive lung disease, either emphysema or alpha-one anti-trypsin deficiency emphysema, will do well with either an SLT or BLT.^{12,13} Selection of one strategy over another has been based on patients' age, size, and co-morbidity with the younger, fitter patients, and those with larger physical stature, receiving BLT. Patients with restrictive lung disease such as idiopathic pulmonary fibrosis, and those with primary or secondary pulmonary hypertension, are similarly eligible for either SLT or BLT. Consideration is given to the technical difficulty encountered while implanting lungs into the small thorax of a patient with pulmonary fibrosis or into the normal sized, but crowded, thorax of a patient with primary pulmonary hypertension who has developed cardiomegaly. A preoperative decision that has been recently encountered is the decision about whether or not the sternum should be divided. Our experience has identified some subsets of patients in whom the sternal sparing clamshell approach may be inappropriate. Patients with secondary pulmonary hypertension due to a cardiac defect may require a full clamshell to allow the concomitant cardiac repair at the time of transplant. Also, patients with a relatively flat anterior-posterior diameter to the chest in whom the heart resides mainly in the left thorax may prove particularly challenging, especially when the left atrial anastomosis is attempted. These patients may be best served by a posterolateral thoracotomy on the left, to avoid excessive anterior retraction on the heart, and an anterolateral or posterolateral incision on the right.

The least functional lung, as determined by preoperative quantitative ventilation and perfusion scans, is resected and replaced first. Replacement of the least functional lung first is important because it increases the likelihood of avoiding cardiopulmonary bypass. An attempt is made to detach all pleural adhesions and fully mobilize the hila of both lungs before the first lung is explanted. This requires careful monitoring of the travel times of the lungs to be implanted are being procured at a remote location and the lung-ischemic time is to be kept at a minimum. This preliminary dissection shortens the time that the first implanted lung is exposed to the entire cardiac output, and thus lessens the likelihood of reperfusion edema in that lung.

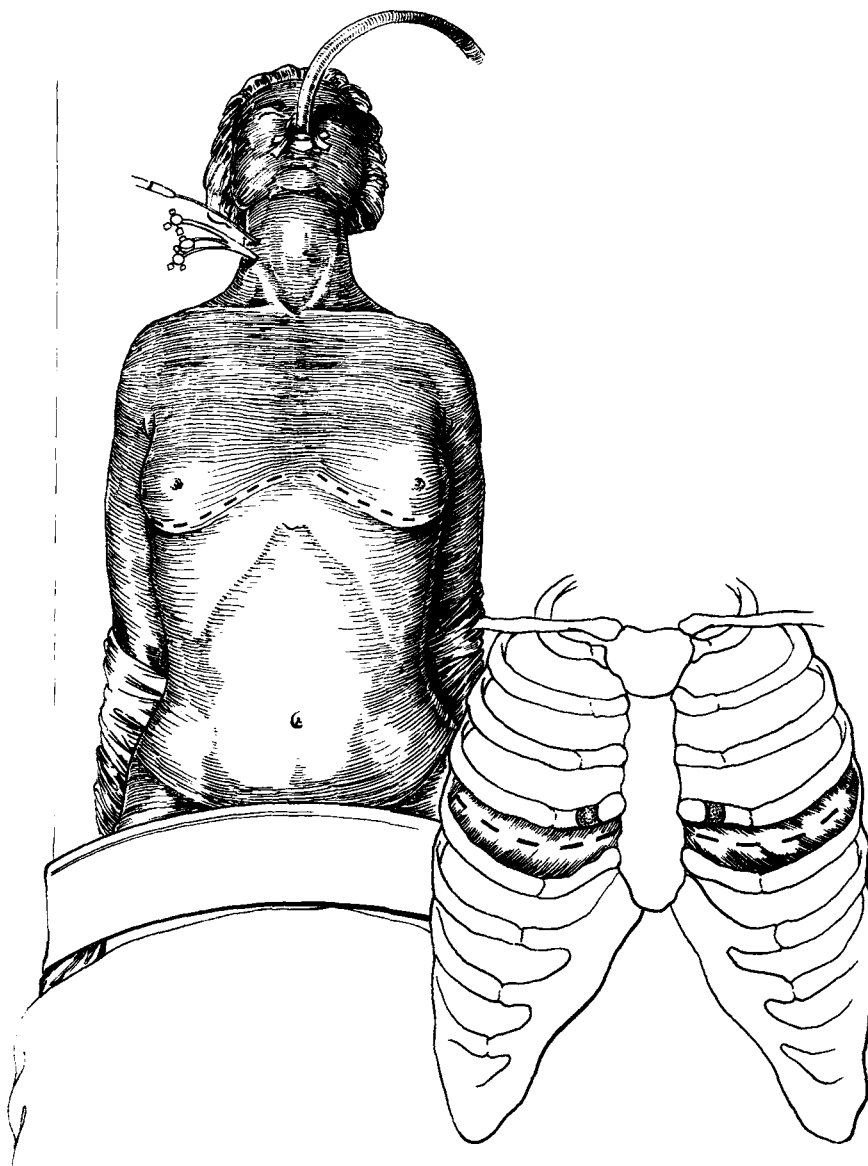
Anesthetic Management

The anesthetic management for lung transplantation is tailored to the particular physiological needs of the transplant recipient. All patients receive a pulmonary artery catheter for monitoring pressures and cardiac outputs during and after the procedure. A multi-lumen central venous catheter is also placed at the same time for administration of intravenous fluids and medications perioperatively.¹⁴

When the indication for transplantation is septic lung disease, the patients are initially intubated with a large single lumen endotracheal tube to allow vigorous suctioning of purulent secretions through an adult bronchoscope. This step is critical in decreasing the tendency of these patients to require cardiopulmonary bypass due to respiratory insufficiency during sequential single lung ventilation. The use of a pediatric bronchoscope or blind suctioning with a catheter through one limb of a double lumen endotracheal tube is insufficient and should not be substituted for the sake of expediency. Patients with emphysema, restrictive disease, or pulmonary hypertension rarely require this step and can be intubated with a standard left-sided double-lumen endotracheal tube at the outset of the procedure.

Blood pressure monitoring is performed with a radial arterial line, though we also place a right femoral arterial line if hemodynamic instability is expected. We have found the femoral line to be more reliable, especially in prolonged, challenging cases in which the use of high-dose pressors is likely. Finally, it is our practice to insert a transesophageal echocardiography (TEE) probe at the start of the procedure. The TEE probe allows for assessment of right ventricular function in the face of dramatically changing pulmonary vascular resistance during and after pulmonary artery (PA) clamping and unclamping. Echocardiography also allows for assessment of air emboli in the left heart after cardiopulmonary bypass and provides additional information about the adequacy of left heart filling and volume status during the transplant operation. Because our cardiothoracic operating rooms are equipped with TEE probes, and our anesthesiologists are skilled in the use of them, routine use of TEE can be performed with little additional risk or expense and no additional personnel.

SURGICAL TECHNIQUE

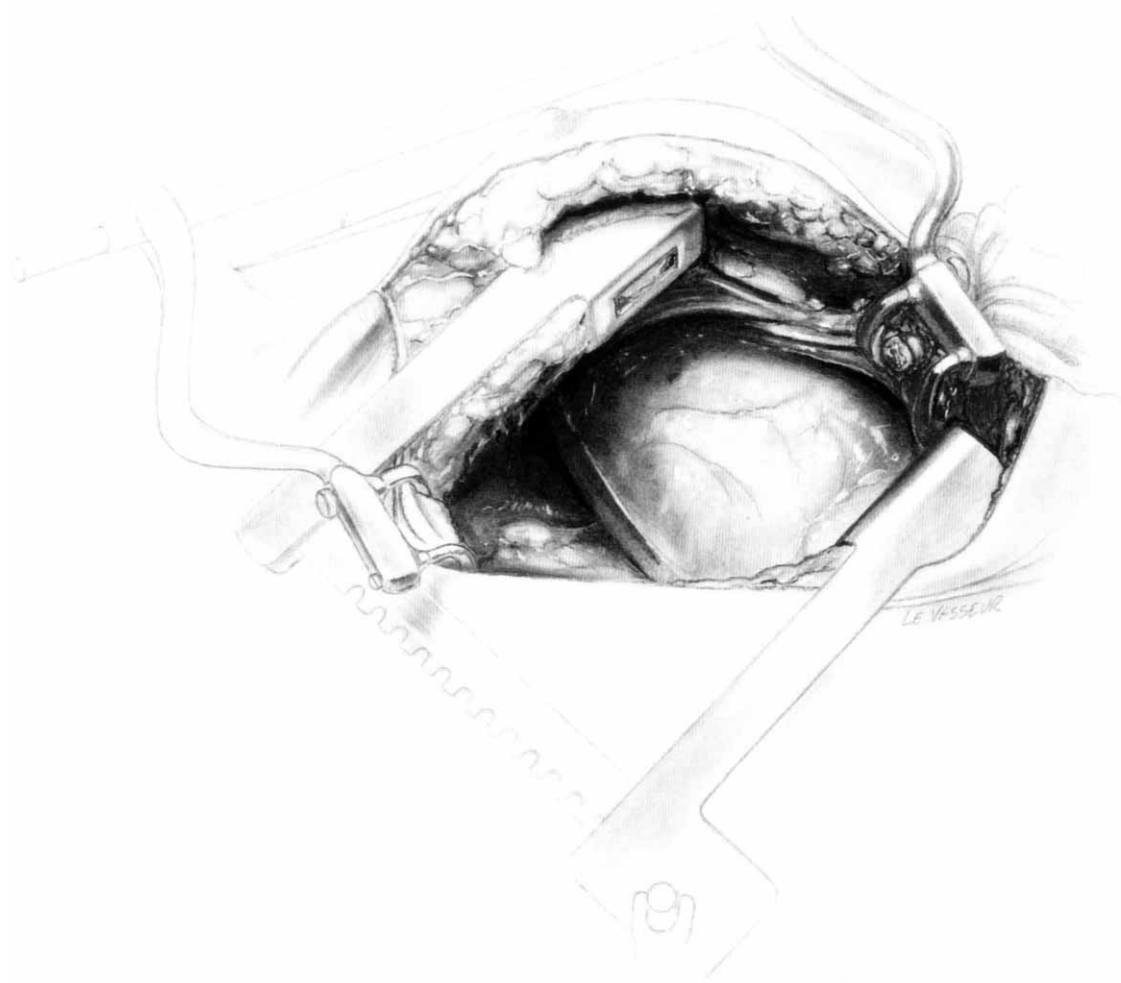


I The patient is positioned supine with all extremities padded and the arms tucked in at the patient's side. We place soft rolled blankets behind the knees to keep the knees slightly flexed. It is important to have the patient securely strapped to the operating table to keep the patient from sliding laterally when the operating table is dramatically tilted left and right to optimize exposure for the hilar dissection and anastomoses.

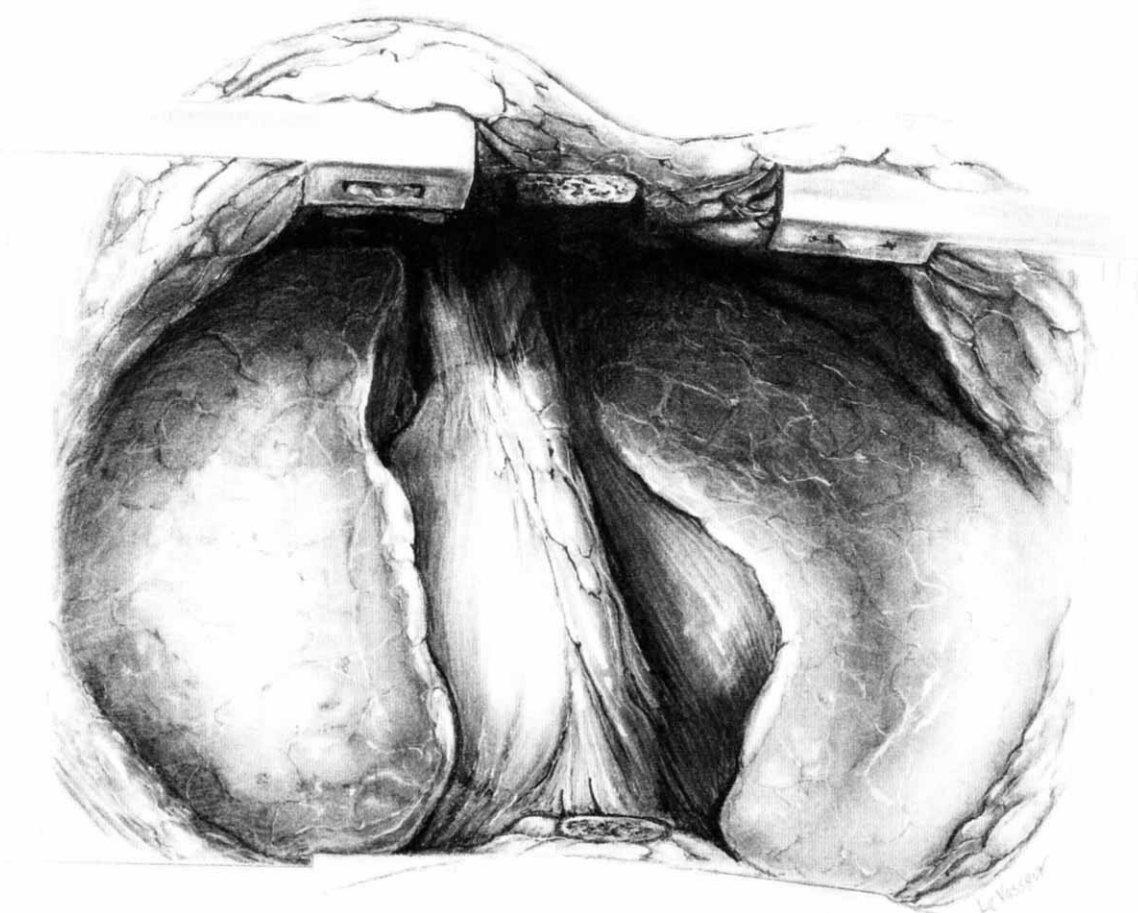
The skin incision runs along the inframammary crease and crosses the sternum at the level of the fourth interspace. Recently, we have omitted the central few centimeters of the skin incision and have used two disconnected anterolateral incisions. The lower edge of the pectoral muscle is divided in the deeper extension of this incision to expose the chest wall. An intercostal incision is made by separating the fourth intercostal muscle from the upper surface of the fifth rib. One centimeter of the costal cartilage of the fourth rib (shaded in diagram) is cleared and eventually resected to allow upward mobility of the fourth rib with application of the rib spreading retractor.



2 A Tudor-Edwards rib shear (V. Mueller, Deerfield, IL) is used to resect a short length of the fourth costal cartilage. The fourth intercostal bundle of nerve, artery, and vein can be doubly ligated and divided to allow free upward movement of the fourth rib. A Finochietto chest retractor is used to spread the ribs vertically. The intercostal muscle division is carried along the upper edge of the fifth rib far more lateral and posterior than limit of the skin incision to maximize rib spreading. The serratus anterior muscle and the long thoracic nerve are not divided; rather, they are pulled away from the chest wall to allow access to the posterolateral intercostal space. In patients with substantial breast tissue, a heavy silk suture is used to temporarily affix the upper edge of the incision to the infraclavicular skin, thereby retracting the breast tissue cephalad and keeping it from falling into the wound.

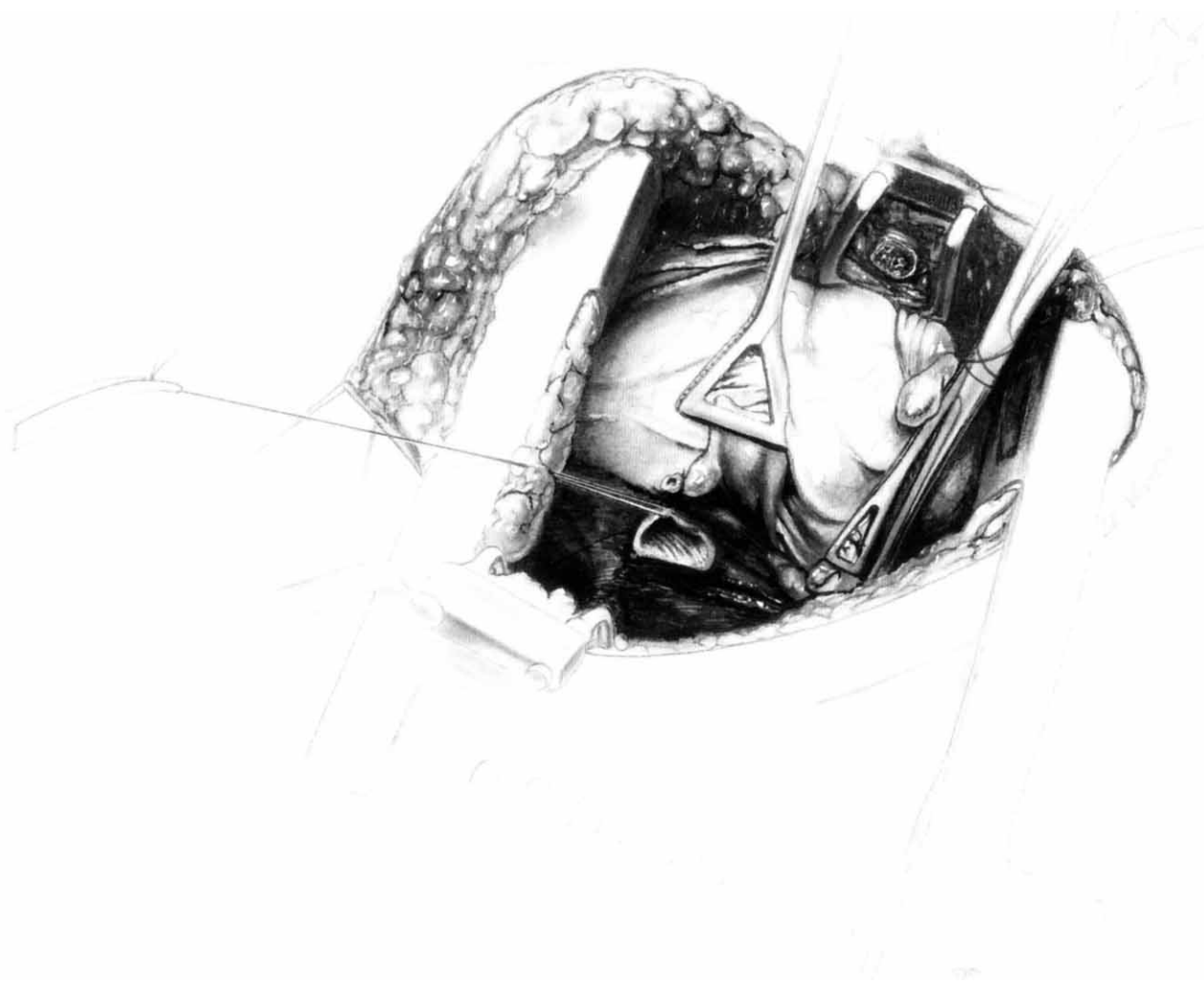


3 A Balfour retractor is placed with a short jaw on the sternum, straddling the cut costal cartilage, and a longer jaw on the muscle and skin of the lateral chest. The combined efforts of the Balfour and Finochietto retractors typically results in excellent exposure without sternal division. More mobility is obtained by dividing the intercostal muscle from within the pleural space. This division can be carried back as far as the sympathetic trunk, which is visible through the pleura. Full extension of this intercostal division has made it unnecessary to remove ribs or to shingle them posteriorly. The only rib division necessary in the vast majority of cases is the anterior fourth costal cartilage.

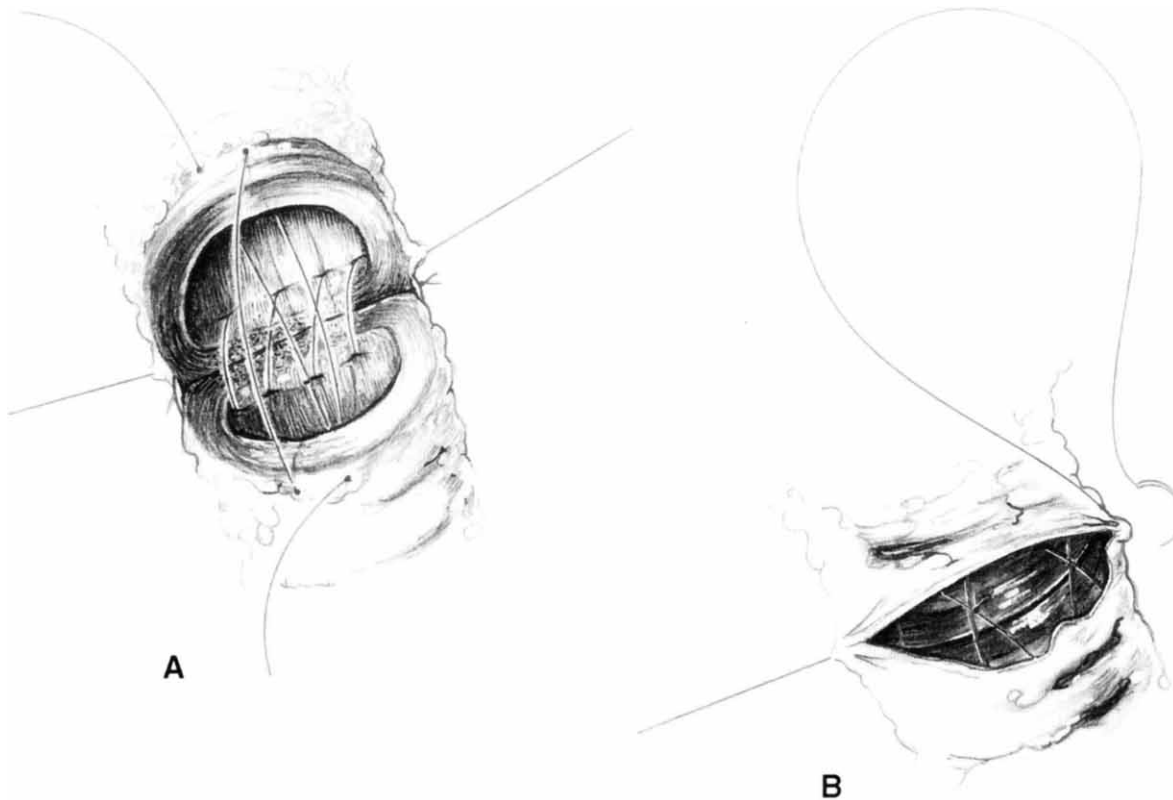


4 Should additional access to the thorax become necessary during the conduct of the operation, the sternum is easily divided transversely at the fourth interspace and the entire chest is opened like a clamshell. In the initial application of this exposure, we found it beneficial to divide the skin overlying the sternum and to ligate and divide the internal mammary arteries bilaterally at the start of the operation to allow expeditious sternal division in the event it became urgently necessary. This conversion to a full “clamshell” has been such a rare event that we no longer include these steps.

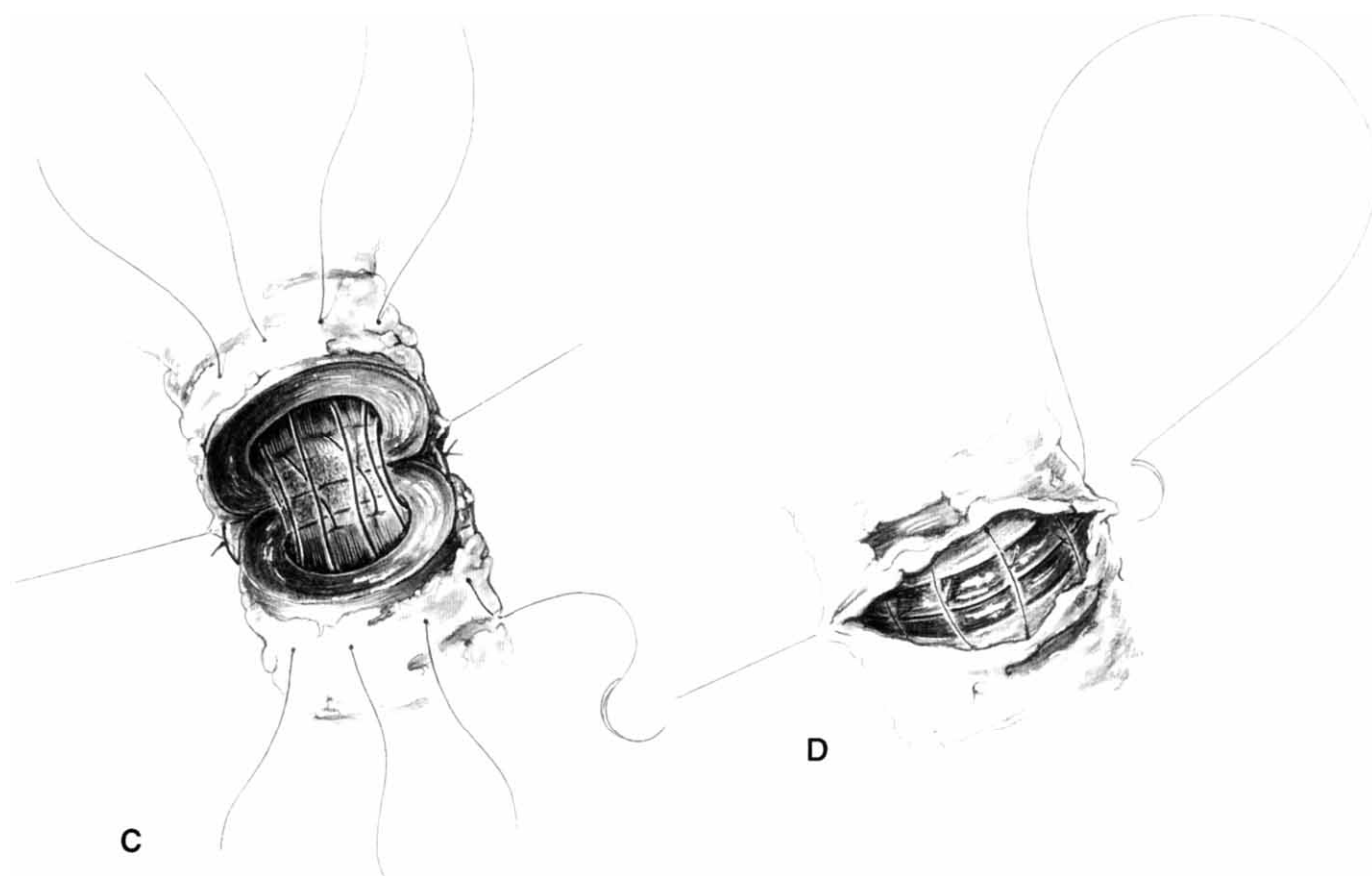
Great care is taken to avoid injury to the phrenic nerve as it passes just anterior to the hilum and to the esophagus, vagus nerve, and thoracic duct, which reside directly posterior. The pulmonary arteries and veins are dissected beyond their primary bifurcations to preserve the length of the main trunks. The right pulmonary artery is usually transected between firings of a vascular stapling device 1 cm beyond the ligated first branch to the right upper lobe. The left pulmonary artery is kept longer and transected between staple lines beyond the second branch to the left upper lobe. The vein branches are usually not stapled; rather, they are ligated and divided at their secondary branch points to save length for the future recipient atrial cuff. The arterial and venous dissection and division is accomplished before the bronchial division to avoid prolonged contamination of the operative field by the open distal airway. The bronchus is transected between cartilaginous rings, and the posterior bundle of lymphatics and bronchial arteries is exposed to facilitate ligation and subsequent division.



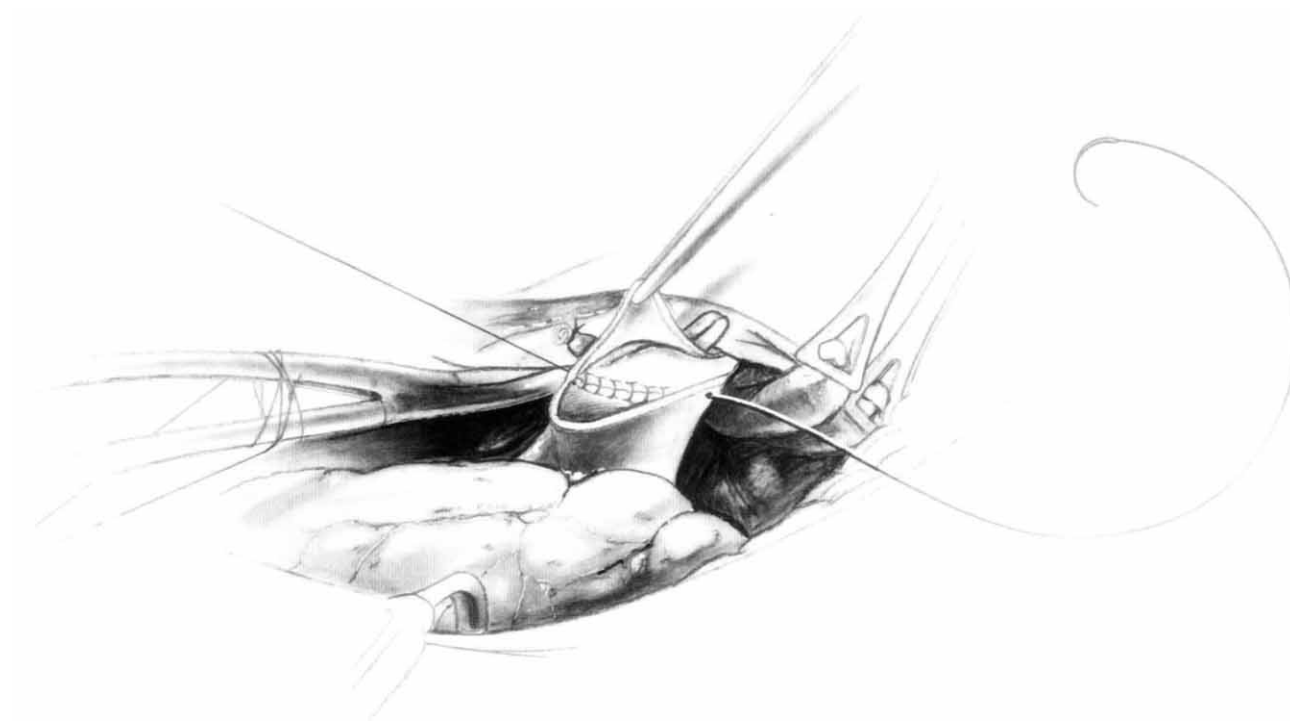
5 The lung is removed from the chest and the field is prepared for implantation of the graft. Self-retaining retractors, fashioned with Duval lung retractors suspended by heavy silk ties, are used to suspend the recipient pulmonary artery and vein medially and anteriorly to expose the bronchus. The pulmonary artery stump is mobilized centrally, then grasped with a clamp and retracted anteriorly to afford better access to the bronchus, which resides to a large extent behind it. The pulmonary vein stumps are then grasped and retracted anteriorly and laterally to permit circumferential opening of the pericardium. Care is taken to avoid creating too large a defect in the pericardium, especially on the right side where cardiac herniation could occur with disastrous results. We try to divide the pericardium at the peripheral reflection on the pulmonary veins and find this is facilitated by the assistant placing a blunt right-angled clamp into the pericardium to define its extent and to lift it off the underlying pulmonary veins. With the pericardium freed, the vein stumps are then retracted and temporarily fixed anteriorly. This provides an excellent view of the bronchus, which is then mobilized well into the mediastinum and divided. Meticulous hemostasis in the posterior mediastinum is achieved at this point, with the knowledge that reaching this portion of the operative field after implantation of the graft lung will be extremely difficult. Finally, a small suction catheter is placed down the appropriate limb of the endotracheal tube until it is just seen within the recipient bronchus. This catheter is useful in removing saline, which accumulates in the thorax from the melting of slush used to keep the graft lung cool during implantation.



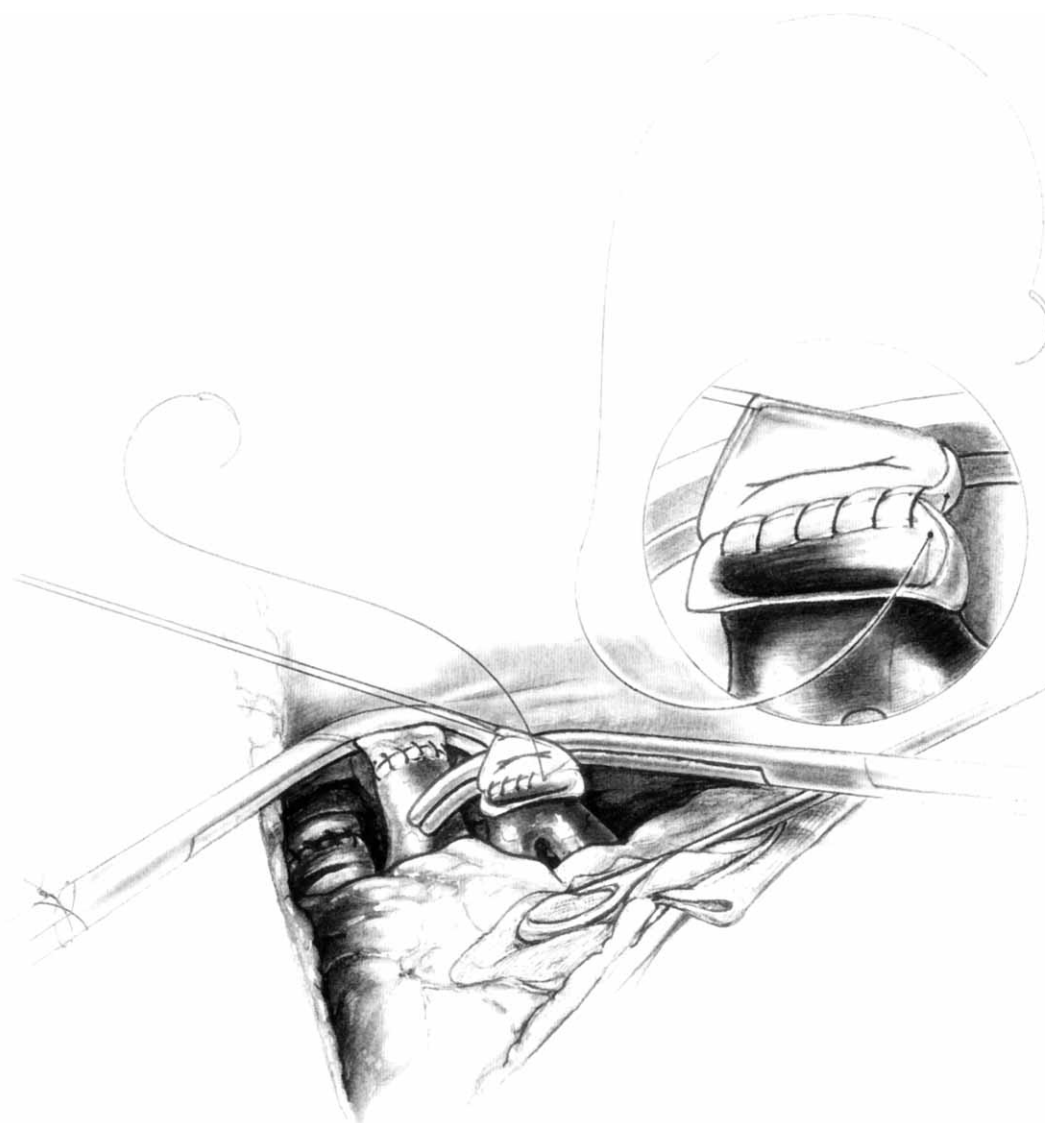
6 The atelectatic graft lung is placed into the chest and kept cold with iced saline and slush. We prefer to conduct the anastomosis from posterior to anterior in the following sequence: bronchus, artery, and atrium. The recipient bronchus is shortened to minimize the risk of ischemia to its distal extent. Ischemia is also avoided by omitting any unnecessary circumferential dissection of the proximal recipient bronchus. The right main bronchus is usually divided two or three cartilaginous rings beyond the carina, whereas the left main bronchus is kept longer. The presence of the left-sided double-lumen endotracheal tube might impair the ability to trim the left bronchus to an appropriately short length, in which case the tube should be backed out a few millimeters by the anesthesiologists. Division of the bronchus should always be at right angles to its axis and between rather than through the cartilaginous rings in order to eliminate the need for any compensatory bevelling of the donor bronchus. The first stitch is a running 4-0 polydioxanone suture (PDS), which unites the peribronchial tissue and lymphatics of the graft to peribronchial tissue surrounding the recipient bronchus. The back wall of this suture is performed just before the bronchial anastomosis and the front wall is performed immediately after the bronchus is closed. The next stitches (A and C) are also 4-0 PDS and they are placed at the two corners of the bronchial anastomosis at the medial and lateral junction of the membranous and cartilaginous airway. These sutures are tied and one end is used to join the donor and recipient membranous airways in a continuous suture.



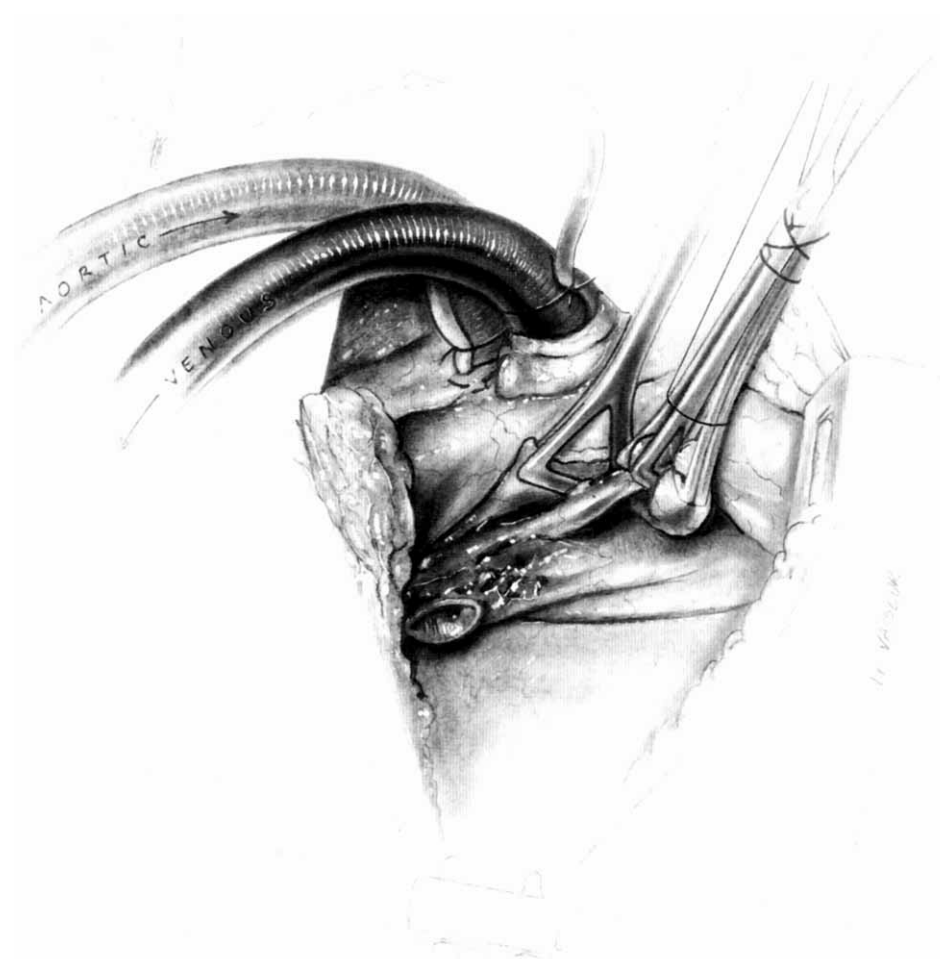
6 (continued) The cartilaginous rings of the donor and recipient are joined with interrupted figure-of-eight 4-0 PDS sutures. This process can usually be accomplished with only five such sutures. Interrupted figure-of-eight sutures (A) are used for bronchial closure in normal or larger than normal sized airways. No attempt is made to intentionally intussuscept the smaller of the bronchial ends into the larger. In smaller airways, particularly left bronchial anastomoses in small recipients, a simple interrupted anastomosis (C) is performed to enhance accuracy and minimize stenosis. The anastomosis is finished with the completion of the anterior half of the peribronchial tissue layer (B and D).



7 The pulmonary artery anastomosis is performed with running 5-0 prolene suture. In the example depicted, the recipient pulmonary artery has been divided distal to the first branch to the right upper lobe. The pulmonary artery, by now, has already been extensively and circumferentially dissected into the mediastinum. The pulmonary artery is then clamped centrally with a Satinsky clamp with care taken to avoid including the pulmonary artery catheter in the jaws of the clamp. The clamp is sewn to the wound edge to immobilize it and to render it less likely to spring open prematurely. The vascular staple line is resected at a location that equalizes the sizes of the donor and recipient arteries. A larger recipient artery can be divided beyond the first ligated branch to match a smaller donor artery, whereas a smaller recipient artery is divided proximal to the first branch, or through it, to maximize circumference. The donor pulmonary artery is trimmed to an appropriate length and the anastomosis is created with running 5-0 prolene suture. This anastomosis must be made with precise, small suture bites to avoid any anastomotic stricture. We generally make this anastomosis with a single continuous suture and have not found it necessary to interrupt the suture line to avoid purse-string narrowing of the anastomosis.



8 The atrial anastomosis is performed last using running 4-0 polypropylene. A Satinsky clamp is placed centrally on the atrium. Placing this clamp too centrally can reduce venous drainage from the contralateral lung and decrease cardiac output, whereas placing the clamp too peripherally will compromise the recipient atrial cuff. Once the clamp is placed, an umbilical tape is used to tie the clamp closed to minimize the likelihood of dislodgement during subsequent lateral retraction of the clamp. The ties are then cut off the recipient vein stumps and the bridge of atrium between vein stumps is divided to create the atrial cuff. Gentle lateral traction on the Satinsky clamp by the assistant can bring this anastomosis to a more accessible location, though we have avoided any fixed retraction because of the consequences of injury to the atrial cuff at the site of the clamp. The left atrial anastomosis is often the most difficult technically, given the propensity of the heart to be in the way. In most cases, however, the suturing can be achieved with maximal tilting of the table to the right, gentle traction on the Satinsky clamp, and gentle medial and anterior retraction of the heart with intermittent release if hemodynamic compromise occurs. The anastomosis is performed with 4-0 prolene suture and the back wall is closed with everting sutures, when cuff length permits, to avoid inverting any cut atrial muscle into the atrium to form a thrombogenic focus. The anterior wall is easily everted with a simple running over-and-over suture line, and the last few sutures are left intentionally loose to allow flushing and de-airing of the graft and the recipient atrium. For this maneuver, the lung is partially inflated and the pulmonary artery clamp is loosened momentarily. The lung is flushed with the atrial clamp still in place to force out the residual pulmonary perfusate solution. The pulmonary artery clamp is then re-applied, and the atrial clamp is opened momentarily to completely de-air the atrium. The atrial sutures are then secured and the clamps are removed. All suture lines are then checked for hemostasis as ventilation and perfusion is restored. An identical procedure is then conducted on the opposite side.



9 The use of cardiopulmonary bypass has decreased dramatically since the early days of lung transplantation. Our preference is to avoid bypass, whenever possible, and thus avoid its potential sequelae of coagulopathy, neurological dysfunction, and renal impairment. The judgment of when to employ cardiopulmonary bypass is based on the data obtained from the pulmonary artery catheter, blood gasses, and the use of a TEE probe. Hemodynamic instability, the inability to adequately oxygenate or ventilate with one lung, dramatic increases in pulmonary arterial pressures with unilateral pulmonary artery clamping, and deterioration of right ventricular function as measured by TEE are all indications for bypass. Some authors have recommended full or partial bypass during the pneumonectomy of the second lung and the implantation of the second graft to avoid flooding the newly implanted lung with the entire cardiac output.^{15,16} The employment of cardiopulmonary bypass ranges from less than 25% of cases in a large adult series to nearly 100% of cases in the pediatric population.^{15,17} Adult patients most likely to require bypass support during transplantation are those with cystic fibrosis, primary pulmonary hypertension, and pulmonary fibrosis.

For conduct of bilateral lung transplant on bypass, our preference is to conduct as much dissection as possible before administration of heparin and cannulation. A two-stage venous cannula is placed in the atrium and an aortic perfusion cannula is placed in the ascending aorta. This is easily accomplished without transverse sternotomy. Femoral cannulation should be avoided to eliminate the complications of a groin incision. For the rare SLT requiring bypass, intrathoracic cannulation is also performed. On the right side, a right atrial cannula is placed and the arterial line is placed in the ascending aorta. On the left side, the proximal pulmonary artery is cannulated for venous drainage, and the descending thoracic aorta provides a good site for arterial line placement. After cannulation, the bypass pump is instituted at full flow and both lungs are excised. After the first lung is implanted, it is left in place with the vascular clamps intact and the atrial suture line untied. The lung is packed in iced saline and slush while the second lung is implanted. Once the second lung is implanted, both lungs are sequentially de-aired and flushed and restoration of perfusion and ventilation occurs essentially simultaneously.

Postoperative Care

At the conclusion of the operation, the double lumen endotracheal tube is exchanged for a large single lumen tube. Fiberoptic bronchoscopy is performed to assess anastomotic patency and donor airway viability, and to suction thoroughly any retained secretions. The patient is transported to the intensive care unit intubated. Mechanical ventilation is continued until the patient is awake and stable and able to be weaned toward extubation. In cases that are not complicated by reperfusion injury, the postoperative care of a BLT recipient is generally smoother than that seen for SLTs. The bilateral lung grafts generally have comparable airway and vascular resistances, so the problem of ventilation-perfusion abnormalities is minimized. Most patients are extubated on the first or second postoperative day. Chest tube management is identical to the practices used after pulmonary resection.

Results

Since July 1988, we have performed 450 lung transplants in 443 patients. The recipients have had a median age of 51 years and the population is evenly distributed between males and females. Recipient diagnoses included emphysema in 229 patients, cystic fibrosis in 70 patients, pulmonary fibrosis in 48 patients, pulmonary hypertension in 49 patients, and miscellaneous (other disorders) in 47 patients. Transplant procedures included SLT in 157 cases, BLT in 283 cases, en-bloc double lung transplant in 8 cases, and heart lung transplant in 2 cases. The use of en-bloc double lung transplantation took place quite early in

our experience with bilateral transplantation and has been completely abandoned and replaced with the bilateral sequential approach.

Four hundred thirteen (91.7%) lung transplant recipients survived to hospital discharge. There were 37 hospital deaths due to sepsis ($n = 6$), cardiac events ($n = 8$), primary graft failure ($n = 8$), anastomotic dehiscence ($n = 6$), and other causes ($n = 9$). Airway anastomotic complications were treated in 55 patients (12%). A diagnosis of chronic allograft rejection/bronchiolitis obliterans syndrome (BOS) has been made in 191 patients (42.5%) and neither the incidence nor the severity of BOS have been improved by any specific therapy. Actuarial freedom from BOS at 1, 3, and 5 years posttransplantation is 82%, 42%, and 25%. Absolute survival of all transplanted patients is 278 patients (62%), with a mean follow-up period of 5.1 years (11 days to 9.3 years). One-, 3-, and 5-year actuarial survival for the entire group is 83%, 70%, and 54%, respectively (Table 1). There is no statistical difference in survival among patients stratified according to diagnosis or according to SLT versus BLT. Waiting time for graft lungs increased steadily from 116 days in the first 90 patients to 634 days in the most recent 90 patients.

Lung transplantation has evolved to become a durable surgical solution to many end-stage pulmonary diseases. Chronic rejection and long waiting lists for donor lungs continue to be major problems facing lung transplant programs. Use of marginal and distant donors are successful strategies in improving donor availability.

TABLE 1. Barnes-Jewish Hospital Lung Transplantation Survival

Years	Bilateral ($n = 285$)	Single ($n = 157$)	COPD ($n = 230$)	CF ($n = 72$)	PF/IPF ($n = 49$)	PH/PPH ($n = 50$)	Other ($n = 43$)	Total ($n = 444$)
1	83	85	87	80	77	78	83	83
2	76	79	83	70	74	70	75	78
3	71	70	77	59	69	66	67	70
4	62	59	64	48	55	66	53	60
5	56	51	53	41	55	63	53	54

Abbreviations: COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; PF/IPF, pulmonary fibrosis, idiopathic pulmonary fibrosis; PH/PPH, pulmonary hypertension, primary pulmonary hypertension.

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